

CASE REPORT

Cryptococcus neoformans meningitis in an immunocompetent adult: A case report

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Abstract: Neuromeningeal cryptococcosis (NMC) is relatively rare in immunocompetent subjects. We report a Congolese case of NMC diagnosed in an apparently immunocompetent subject. A 35-year-old woman was admitted for acute meningoencephalitis. The cerebrospinal fluid (CSF) examination revealed cytological and biochemical abnormalities and the presence of *Cryptococcus neoformans* on direct examination with India ink and in culture. The serum dosage of cryptococcal antigens was titrated at 1:32. HIV and syphilis antibodies were negative and the blood CD4 lymphocyte count was 610/mm³. The patient had no other immunosuppressive factors, in particular no hematologic abnormalities, no solid tumor, or malnutrition. She was unsuccessfully treated with fluconazole intravenously, and died after 10 days of treatment. This observation reminds us that NMC can occur in subjects without apparent immunosuppressive factor with a misleading clinical presentation. It is a rare infection with a severe prognosis even in immunocompetent patients.

Keywords: cryptococcosis, immunocompetent, meningoencephalitis

1 Introduction

Cryptococcosis is an infection caused by the yeast, *Cryptococcus neoformans*, which readily enters the body through the respiratory tract. Its localization is multisystemic; however, this yeast has a marked tropism for the central nervous system, causing meningoencephalitis^[1,2]. It often occurs in an immunocompromised area and is often associated with human immunodeficiency virus (HIV) infection, of which it is one of the first opportunistic infections^[3]. However, neuromeningeal cryptococcosis (NMC) is rare in immunocompetent subjects^[4]. We report a case of a young woman, without an obvious immunosuppressive factor, admitted with a clinical picture of meningoencephalitis, in whom the diagnosis of NMC was made on the basis of the presence of cryptococci in the cerebrospinal fluid (CSF), and serum cryptococcal antigen assay.

2 Clinical observation

A 35-year-old Congolese woman with no profession is brought in by her family for behavioral problems. The onset of symptoms dated back two weeks after the present consultation with fever and occipital headaches, intense and intermittent, radiating to the neck. Antimalarials and analgesics prescribed in different health facilities did not bring any clinical improvement. After a week, psychomotor restlessness appears. Her medical history is unremarkable. Neither hemopathy, solid tumor, malnutrition, diabetes mellitus, or any other obvious factor of immunosuppression was found in her.

Her general state was marked by a feverish state (temperature at 39°C). The physical examination revealed frank meningeal syndrome with stiff neck, signs of Kernig and Brudzinski. The remainder of the physical examination was normal, and in particular, there was no splenomegaly, hepatomegaly, pleuropulmonary or cardiac abnormality. The lumbar puncture showed a clear fluid with an average cellularity (45 elements/mm³) predominantly lymphocytic, hypoglycorachia, and hyperproteinorachia. Direct mycological examination with India ink of the CSF found the presence of numerous *Cryptococcus neoformans*, whereas bacteriological examination was normal. Serum assay of cryptococcal antigens gave a titration of 1:32. Complete blood count showed hyperleukocytosis at 11,950 elements/mm³ predominantly

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neutrophilic (84%), and a sedimentation rate of 103 in the first hour. Hemoglobin level, renal (urea, creatinine), carbohydrate and lipid balance as well as the protein level are normal. Brain imaging was normal. HIV and syphilis antibodies were negative, and the blood CD4 lymphocyte count was 610 /mm³. The diagnosis of neuro-meningeal cryptococcosis in an immunocompetent patient was confirmed. In the absence of amphotericin B, treatment with fluconazole was immediately started intravenously at a dose of 600 mg per day. Despite this treatment, the patient's condition continues to worsen. The evolution was marked by death in this context of deterioration of the general condition on the 10th day of treatment.

3 Discussion

Cryptococcosis is a very opportunistic yeast that occurs in subjects with severe immunodeficiency, especially in HIV-infected subjects with a CD4 count below 200 /mm³[1,3]. It is a serious fungal infection, in particular because of its neuro-meningeal tropism. Its diagnosis is difficult in the absence of a favorable factor at first glance[3,5]. It is a sporadic disease before the onset of HIV infection, and its incidence has increased considerably since 1980[6].

NMC is manifested by meningoencephalitis. The clinical manifestations are nonspecific, often misleading, and their expression ranges from simple long-term fever to fulminant meningitis. This makes the clinical diagnosis of this pathology problematic[1,7,8]. Febrile neurologic syndrome is more suggestive and includes paralysis of the cranial nerves (especially facial and oculomotor nerves), paresis of a limb, seizures, change in mood, and behavioral disturbance. It is noted in 20 to 50% depending on the series[6]. In our case, only fever, headache, behavioral disorder and meningeal syndrome were clinically found. In their study carried out in Morocco in 2017, Chadli *et al.*[9] found no cases of seizures and damage to cranial nerves in 40 cases of NMC.

Cryptococcosis preferentially affects the central nervous system and presents as meningoencephalitis in 69% of non-HIV-infected subjects and 90% of HIV-infected subjects[10]. Faced with any clinical picture of meningoencephalitis, it is therefore necessary to look for acquired immunosuppression linked to HIV.

However, NMC leads to diagnostic delays when the risk factor is not clearly identified[5]. In our case, the patient had no identified risk factors or immunosuppression grounds. It was the neuro-meningeal clinic as well as the result of CSF analysis that enabled us to retain the diagnosis of NMC.

NMC characterizes the advanced stage of immunosuppression. It occurs in 80% of cases in people with severe cellular immunosuppression with a median CD4 lymphocytes of 8 cells/mm³. However, cases of NMC occurring in patients with CD4 counts above 200 /mm³ have been reported[11,12], suggesting that this condition is possible even in stages of moderate immunosuppression. In our patient, we found a normal CD4 count at 610 /mm³. Emergency diagnosis of NMC is based on the search for yeasts in the CSF and for circulating antigens. Direct microscopic examination is positive in 72 to 84% of cases, only its sensitivity is not as certain as that of CSF culture which varies from 94 to 100%[9,12].

Serum screening for cryptococcal antigens generally has excellent specificity and sensitivity (> 95%). In addition, the method is simple, fast and reliable, which makes it the means of choice for the diagnosis of NMC[9]. The antigen titer reflects the fungal load, offers better monitoring of treatment[14], and is correlated with the degree of severity of the infection[10]. The dosage of this antigen in the blood was positive in our patient with a titration of 1:32. The diagnosis was made on analysis of the CSF which shows a slight hypercellularity, a slight hyperproteinorrachia as well as a moderate hypoglycorrachia. The same results were found in the cases described by several authors[5,8,10]. Direct examination with India ink reveals numerous cryptococci. This test is positive in 80% of cases in HIV-infected subjects and in 30 to 50% of cases in non-HIV-infected subjects[15]. Immunologically, the CD4 count was 610 /mm³ and the HIV ELISA test was negative. We also noted a hyperleukocytosis at 11,950 predominantly neutrophilic (84%), the sedimentation rate was high at 103mm per hour. The brain scan was normal in our case. In the literature, normal brain imaging is found in 50% of cases for brain CT-scan[5,9]. Therapeutically, our patient was put on fluconazole. This medication was used in the cases described by Bamba *et al.*[11] in their study. In contrast, in other studies, the initial treatment relied on the administration of amphotericin B because of its lower cost in several regions[8,14] before switching to fluconazole. The course of our patient was marked by death. In several studies, mortality was higher than survival despite high doses of fluconazole[8,15].

4 Conclusion

NMC is an uncommon condition in the immunocompetent subject. It is important to think about it and to look for it systematically in front of any meningoencephalitis which does not prove its point, even in an immunocompetent subject, especially since there are treatments which

can be effective if taken in time.

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